

Correspondence

Cutaneous thrombosis associated with skin necrosis following Oxford-AstraZeneca COVID-19 vaccination

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Dear Editor,

A 73-year-old man presented with ulceration of his left shin 2 weeks after receiving his first dose of the ChAdOx1 nCov-19 (Oxford-AstraZeneca) COVID-19 vaccine. He had a background of atrial fibrillation with ischaemic cardiomyopathy and had been on several longstanding medications, including apixaban. Within 24 h of vaccination, he had become generally unwell with fever and headache. After resolution of these systemic symptoms, on the third day after vaccination, he developed left shin erythema and blistering, which rapidly ulcerated (Fig. 1).

On physical examination, the patient was found to have two superficial ulcers with a necrotic base and a violaceous edge, which measured approximately 20 × 30 mm, on the lateral aspect of his left shin.

Blood tests revealed normal liver and renal function tests with normal levels for antinuclear antibodies, antineutrophil cytoplasmic antibodies, prothrombin time, activated partial thromboplastin time, fibrinogen and D-dimer. Full blood count showed a normal white cell differential count and mild thrombocytopenia (platelets $112 \times 10^9/L$; normal range: $150\text{--}450 \times 10^9/L$); the latter had been intermittently present at similar levels over the preceding 12 months but had not been previously investigated.

The differential diagnosis included pyoderma gangrenosum, vasculitic ulceration and a cutaneous adverse drug reaction to vaccination.

A punch biopsy was obtained from the edge of an ulcer, which revealed microthrombi within blood vessels, an ischaemic epidermis and fat necrosis of subcutaneous tissue (Fig. 2).

The patient experienced slow healing of ulceration with topical clobetasol propionate 0.05%, neomycin sulfate and nystatin ointment, along with compression bandaging treatment. To complete the vaccination schedule, the second dose was switched to the Pfizer COVID-19 vaccine, which the patient received with no complications, 12 weeks after his first vaccination.

Several types of vaccination have been developed against the SARS-CoV-2 virus as part of public health



Figure 1 (a–c) Evolution of clinical features on lateral aspect of left shin on (a) Day 3, (b) Day 7 and (c) Day 21 post-ChAdOx1 nCov-19 (Oxford-AstraZeneca) vaccination.

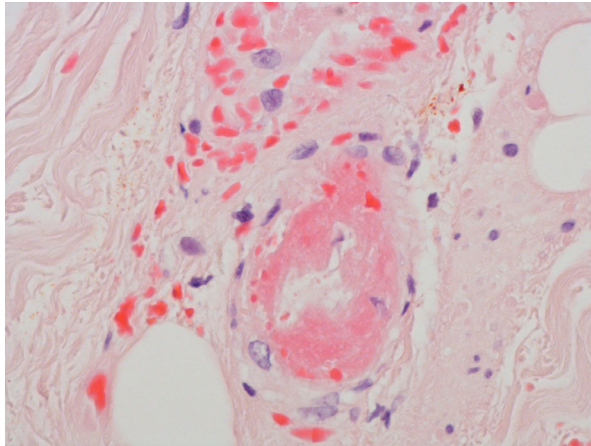


Figure 2 Skin biopsy showing epidermal necrosis with underlying proliferation of blood vessels, many of which show the presence of microthrombi. Fat necrosis also evident in the subcutaneous tissue. Haematoxylin and eosin, original magnification $\times 400$.

strategies in the current COVID-19 pandemic. The ChAdOx1 nCov-19 vaccine delivers the SARS-CoV-2 spike protein DNA within a nonreplicating recombinant chimpanzee adenovirus vector system.¹ Recently there have been concerns related to rare reports of thrombotic events at atypical sites (including cerebral and splanchnic vascular beds) associated with thrombocytopenia following ChAdOx1 nCov-19 vaccination (termed 'vaccine-induced immune thrombotic thrombocytopenia').²

The mechanism of thrombotic events secondary to ChAdOx1 nCov-19 vaccination remains unknown. SARS-CoV-2 infection itself is associated with hypercoagulability, with a high incidence of venous thromboembolism.³ Vaccine-induced thrombotic cases exhibit similarities to those with heparin-induced thrombocytopenia, notably the presence of serum antibodies against platelet factor 4.² This is hypothesized to cause platelet activation and stimulation of the thrombotic cascade to create a pro-thrombotic state.⁴ Whether these changes are initiated by the presence of free DNA in the vaccine, factors related to the viral vector system, or the spike protein triggered immune response are yet to be elucidated. Furthermore, it is also currently unclear why this immunogenic

thrombotic phenomenon preferentially manifests at certain sites.

To our knowledge, this is the first reported case of cutaneous thrombosis associated with skin necrosis following ChAdOx1 nCov-19 vaccination. These findings extend the range of atypically located thromboses associated with COVID-19 vaccination. This case reinforces the necessity for physicians to be vigilant for signs and symptoms related to thromboses at atypical sites in recently vaccinated patients.

Acknowledgement

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